

PATENT

Case: 027664 (formerly 01288)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF
Steven MacLeod

GROUP ART UNIT: 3761

SERIAL NO: 10/644,516

EXAMINER: Leslie Deek Switzer

FILED: 08/20/2003

DATE: 08/11/2006

TITLE: INJECTABLE PHARMACEUTICAL SUSPENSION IN A TWO-CHAMBER VIAL

RESPONSE TO FINAL OFFICE ACTION

Commissioner of Patents
P. O. Box 1450
Alexandria, VA 22313-1450

Dear Sir/Madam:

This is in response to the Office Action of 16 March 006, having a period for Reply set to expire on June 16, 2006. A two-month Extension of Time to August 16, 2006 is hereby requested. Also submitted herewith are a Notice of Appeal and a corrected Figure 2.

Amendments to the Drawings A substitute drawing labeled "REPLACEMENT SHEET" is attached herewith.

Remarks/Arguments begin on page 2

Drawings

The Examiner objected to the drawings received from applicant on 20 January 2006. The Examiner notes while the replacement drawing corrects the objections noted in the Office Action mailed 20 October 2005, the replacement FIG 2 is unclear, since the figure overlaps the reference numerals on the right side, rendering the designations unclear. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action.

Applicants have submitted herewith a replacement drawing, labeled "Replacement Sheet" in which the reference numerals do not overlap the figure.

Claim Rejections - 35 USC § 103

Claims 1-3 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 4,089,432 to Crankshaw et al.

The Examiner contends that Crankshaw discloses the structure of a vial 11 with two chambers 13, 14, a stopper 17 intermediate the chambers, and an upper stopper 23. Crankshaw discloses that movement of the upper stopper is an actuating means that pushes the intermediate stopper out of its seal with the constricted portion 16 of the vial, allowing the contents of the two chambers to mix within the combined volume of the two chambers. Crankshaw further discloses the cap 44 over the top of the stopper, a thin wall of the stopper for needle piercing, and the connections, sleeves, and locks of the claimed vial (see, generally, columns 2-4).

The Examiner admits Crankshaw fails to disclose that the upper chamber is filled with an aqueous medium and the lower chamber is filled with a gaseous medium. To overcome this element of the present invention the Examiner argues that the purpose of the two-compartment vial is to provide a stable storage solution wherein two substances, which may include a medication and may be stored completely independently from one another. The Examiner maintains Crankshaw discloses that in a preferred embodiment, the upper compartment is filled with a powdered medication and the lower chamber is filled with a solvent. The Examiner asserts Crankshaw specifically discloses that the preferred embodiment is only one utilization of the invention, thereby contemplating

other solutions or compositions in the chambers of the vial (column 3, lines 42-45). To support this position the Examiner avers it has been held that a) the mere reversal of the essential working parts of a device involves routine skill in the art, and b) omission of an element and its function in a combination where the remaining elements perform the same function as before involves only routine skill in the art.

The Examiner concludes it would have been obvious to one having ordinary skill in the art at the time the invention was made to provide a medicament in solution in one chamber, separated from a dehydrating gaseous medium (absent any lyophilized medicament) in the other chamber, as claimed, since the separation of the two components until just before use improves the stability and the shelf life of the mixed solution, as taught by Crankshaw.

Applicant respectfully submits that the examiner has failed to establish a *prima facie* case of obviousness. To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). Contrary to the holding of the Examiner, applicant respectfully submits that the Examiner has failed to establish a *prima facie* case of obviousness because the Examiner has failed to fulfill these requirements.

First, the Examiner has failed to show that all of the claim limitations are taught or suggested. The Examiner has not shown that Crankshaw teaches a gas impermeable septum separating the aqueous compartment from the gaseous compartment. The Examiner has totally ignored this limitation of the claim.

Second, the Examiner has failed to establish that there is some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference. While the Examiner admits

that Crankshaw only discloses that the upper compartment is filled with a powdered medication and the lower chamber is filled with a solvent, the Examiner relies on Crankshaw statement that the illustrated embodiment is only one utilization of the invention, thereby contemplating other solutions or compositions in the chambers. The issue is not whether the art contemplated other combinations but whether the art contemplated the claimed combination. The Examiner has failed to establish that there is any teaching or suggestion of the particular combination claimed (ie liquid/gas - separated by a gas impermeable membrane). Mere contemplation does not constitute motivation – to the contrary there must be clear blaze marks marking the trail thru the woods. Crankshaw doesn't provide such blaze marks.

Third, the Examiner has failed to show there is a reasonable expectation of success. The Examiner argues that one skilled in the art would have substituted the lyophilized drug component separated from the aqueous medium by a moisture barrier of Crankshaw with the aqueous drug component and gaseous component of the present invention. However, the Examiner has failed to establish that there was a reasonable expectation of success that the moisture barrier of Crankshaw would effectively serve as a gas impermeable barrier between a gas and a drug containing aqueous medium of the present invention.

In determining the differences between the prior art and the claims, the question under 35 U.S.C. 103 is not whether the differences themselves would have been obvious, but whether the claimed invention as a whole would have been obvious. *Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530, 218 USPQ 871 (Fed. Cir. 1983); *Schenck v. Nortron Corp.*, 713 F.2d 782, 218 USPQ 698 (Fed. Cir. 1983).

The Examiner's distillation of the present invention down to the mere "gist" or "thrust" of just a two-compartment vial to provide a stable storage solution wherein two substances, which may include a medication disregards the requirement that the subject matter must be analyzed "as a whole" (see *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303).

The present claim is directed to a plural compartment mixing vial wherein a center plug placed between two compartments for temporarily isolating a liquid-

containing compartment from a gaseous medium. The present claim differs from the prior art in the selection of a gas impermeable septum separating an aqueous suspension comprising i) an aqueous medium; ii) a drug in solid particulate form; iii) a wetting and/or suspending agent – at least one of the ingredients being susceptible to oxidation; from a gaseous compartment compared to a moisture barrier separating an aqueous compartment from a lyophilized component. In the present invention a dual chamber vial configuration was discovered where a drug substance in solid particulate form could be stored in an aqueous medium providing controlled flocculation and eliminating the head space in the compartment to prevent oxidation of an ingredient in the formulation and providing a second compartment comprising a gaseous component separated from the aqueous compartment by a gas impermeable septum which when breached provides a headspace for agitation of the formulation. The problem to be solved - a vial configured to prevent oxidation of an ingredient and to create a headspace to allow agitation of the formulation just prior to administration was not envisioned by the prior art. The problem to be solved is part of the invention as a whole. "[A] patentable invention may lie in the discovery of the source of a problem even though the remedy may be obvious once the source of the problem is identified. This is part of the 'subject matter as a whole' which should always be considered in determining the obviousness of an invention under 35 U.S.C. § 103." *In re Spinnoble*, 405 F.2d 578, 585, 160 USPQ 237, 243 (CCPA 1969).

The present invention when taken as a whole is not a reversal of the essential working parts of a device as suggested by the Examiner. The whole of the present invention is more than the reversal of two compartments separated from each other. The present invention includes components (liquid formulation separated from gas) not specifically disclosed by Crankshaw and no means to separate them (gas-impermeable septum). Likewise, the present invention is not an omission of an element and its function in a combination where the remaining elements perform the same function as before. The elimination of the moisture barrier of Crankshaw does not result in a device that functions as a gas impermeable barrier of the present invention.

Crankshaw does not disclose or suggest the invention as a whole as claimed. Applicants submit that the Office has failed to establish a *prima facie* case of obviousness and request that the rejection be withdrawn.

Claims 5-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 4,089,432 to Crankshaw et al in view of US 6,481,435 to Hochrainer et al.

The Examiner argues Crankshaw discloses the device substantially as claimed with the exception of the contents and relative formulations of the medicament within the vessel. Hochrainer discloses that steroids such as, for example, clobetasol and meprednisone, among others, are often packaged in two-chambered dispensing vials in suspensions for administration to a patient in various concentrations (see column 4, lines 5-12, 38-50, columns 5-6).

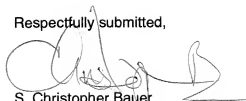
The Examiner concludes it would have been obvious to one having ordinary skill in the art at the time the invention was made to supply the vial disclosed by Crankshaw with a desired medicament for a particular medical treatment, since it has been held to be within the general skill of a worker in the art to select a known material on the basis of its suitability for the intended use as a matter of obvious design choice. See MPEP 2144.07, citing *In re Leshin*, 125 USPQ 416.

For the reasons set forth above and previously presented Crankshaw does not make obvious the presently claimed invention. The teachings of Hochrainer do not overcome the shortcomings of Crankshaw. Hochrainer discloses a two chamber nebuliser configuration where the solvent is kept separate. It is interesting to note that Hochrainer can also be simplified to a two-compartment vial to provide a stable storage solution wherein two substances, which may include a medication, and may be stored completely independently from one another and non-obvious over Crankshaw. However, such a distillation of Hochrainer would also be improper.

Hochrainer in view of Crankshaw does not disclose or suggest the invention as a whole as claimed. Applicants submit that the Office has failed to establish a *prima facie* case of obviousness and request that the rejection be withdrawn.

In view of the foregoing it is respectfully submitted that the pending claims are in condition for allowance. Therefore, reconsideration and swift passage of the application and claims to issue are respectfully requested.

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'S. Christopher Bauer', with a long horizontal flourish extending to the right.

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Attachment: "Replacement Sheet" of Figure 1 & 2